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Magnetic Resonance Imaging: Controlled Interstitial Laser Therapy in Children With Vascular Malformations

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Background and Objective: **Interstitial laser therapy (ILT) is a minimally invasive treatment method for congenital vascular malformations (CVM). This study was intended to show whether or not open magnetic resonance imaging (MRI) offers a means of on-line thermometry and procedure control.**
Study Design/Patients and Methods: **ILT using a bare fiber and an Nd:YAG laser was applied in 20 children with CVM under open MR-control.**
Results: **With the open MR-systems, needle placement and advancement was excellent in all cases. On-line thermometry was possible in 90% of the therapy spots. The 6 week MR follow-up revealed a 76% reduction in tumor size in 14 patients. Clinical symptoms improved in 85% of the patients.**
Conclusion: **MR-guided ILT could become a safe method to treat selected types or selected regions of CVM. Lasers Surg. Med. 23:250–257, 1998.**

Key words: **congenital vascular disease; interstitial thermotherapy; minimally invasive procedure; Nd:YAG laser; open magnetic resonance imaging**

INTRODUCTION

Congenital vascular malformations (CVM) may become symptomatic due to expansive volume enlargement, compression, and infiltration of adjacent structures. CVM are divided in groups according to the Hamburg classification [1]. Type, localization, and extension are decisive factors for the therapy protocol which is interdisciplinary and multimodal. Conservative, interventional, and open surgical procedures are applied. CVMs which have a clear boundary to the surrounding structures or which have large arteriovenous shunts should be resected surgically, possibly with a selective embolization directly prior to surgery. But in the case of a diffuse and infiltrating tumor growth, there is a risk of damage to neighboring structures, resulting in a high recurrence rate due to the lack of radical surgery. This was the reason for investigating less invasive palliative procedures such as interstitial laser therapy (ILT) for these forms of CVM.

Interstitial laser therapy (ILT) is a minimally invasive treatment procedure used to create thermal lesions in pathological tissue and has frequently been applied for different indications. The first interstitial laser application was done in a child described by Ascher in 1983, treating a cerebral tumor under magnetic resonance imag-

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TABLE 1. Characteristics of the Patients and the Associated Congenital Vascular Malformations

Child	Age[a]	Sex[b]	Diagnosis	Flow	Location	Symptoms
1	8	M	Extratruncular venous CVM	Low	Thigh	Pain, palsy
2	2	F	Extratruncular arterial CVM	High	Retroperitoneal	Severe scoliosis, pain
3	11	F	Extratruncular lymphatic CVM	No	Retroperitoneal	Scoliosis, pain
4	1	F	Extratruncular venous CVM	Moderate	Neck	Stridor
5	12	F	Extratruncular lymphatic CVM	No	Retroperitoneal	Scoliosis, pain, palsy
6	2	F	Truncular arteriovenous CVM	High	Mediastineal	Thrombopenia
7	6	M	Extratruncular venous CVM	Low	Thigh	Pain, weakness
8	14	F	Extratruncular venous CVM	Low	Gluteal	Pain, paresthesia
9	14	M	Extratruncular venous CVM	Low	Thigh	Pain
10	1/4	F	Truncular arteriovenous CVM	High	Neck	Stridor
11	1/2	F	Extratruncular arteriovenous CVM	Moderate	Neck	Rapid growth
12	14	F	Extratruncular hemolymphatic CVM	Moderate	Presacral	Bleeding
13	14	F	Extratruncular hemolymphatic CVM	Moderate	Pelvis	Bleeding
14	3	F	Hemangioendothelioma	High	Retrosternal	Pleural effusion
15	5	M	Extratruncular venous CVM	Low	Leg	Pain, weakness
16	3	F	Hemangioendothelioma	High	Diaphragmal	Thrombopenia, pain
17	17	F	Extratruncular arterial CVM	Moderate	Leg	Pain, weakness
18	8	F	Extratruncular arteriovenous CVM	Low	Thigh	Pain, weakness
19	8	F	Extratruncular hemolymphatic CVM	Moderate	Pelvis	Bleeding
20	14	M	Extratruncular lymphatic CVM	No	Retroperitoneal	Severe scoliosis, pain

[a]years.
[b]F = female; M = male.

ing (MRI) control [2]. Other groups applied interstitial laser therapy to treat liver tumors [3–7], benign prostatic hyperplasia [8–10], head and neck tumors [11,12], and breast cancer [13,14]. Only a few papers are related to the laser treatment of vascular malformation [15–17], showing that ILT provides denaturation of tissue and subsequent obstruction of vessels.

For ILT a quartz fiber is directly positioned within the tumor or vascular malformation and a near infrared laser is used at moderate power settings. The distal fiber end can be prepared as a bare fiber with a forward directed radiation characteristic. The advantage of the bare fiber is its small diameter (< 1 mm, including coating) allowing the use of thin puncture needles for placement; its disadvantage is the tendency to induce carbonization due to high power densities at the fiber tip [18]. Alternatively, the distal end can be prepared in order to diffusely distribute the laser light within the region of interest (diffusing tip, scattering applicator). The power density is essentially reduced by the large radiating surface, allowing for higher laser powers without carbonization [19,20]. Consequently, larger volumes of denaturation may be achieved. The disadvantage of diffusing tips is their larger diameter (typically 2 mm), requiring special interventional techniques for the percutaneous approach.

The interventional application of laser energy requires an adequate monitoring procedure. Whereas MRI has already proven to be an effective method to monitor interstitial laser coagulation [21], the development of open MR-systems provides interventions within the measuring volume [22]. One substantial advantage of MRI is the improved soft tissue characterization, providing a precise needle positioning in the tumor [23]. Furthermore, the method is sensitive to thermal- and perfusion-related changes [23,24]. In the absence of ionizing radiation, diagnosis, treatment monitoring, and follow-up control can be carried out using only one system [25]. Hence, the pilot clinical study presented here was intended to show whether open MR-controlled ILT might become a complementary or alternative therapeutic procedure for the treatment of CVM.

MATERIALS AND METHODS

Patients

From February 1996 until January 1998 a total of 20 MR-guided laser interventions were carried out on children aged from 3 months to 17 years (Table 1). Reasons for the intervention were always malformation-related symptoms. All treated CVMs showed an infiltrating and a displacing growth whereas clearly demarcated CVMs were no indication for ILT. Color coded duplex sonography (CCDS) enabled a grading of the CVM into four classes, based on the measured

blood perfusion rate. All treatments were carried out under general anesthesia, three children received an angiographic embolization directly before the laser intervention in order to reduce the CVM perfusion (patients 6, 10, and 14). All children received perioperative antibiotic prophylaxis for 3 days (Cefotiam 50 mg/kg b.w./d and Gentamycin 5 mg/kg b.w./d).

Laser and Monitoring System

The applications were executed with a Nd:YAG laser (1,064 nm, Fibertom 5100, Dornier, Germany) which was set up in the MR control room. The laser was equipped with a light-guide protection system (LPS) that detects huge carbonization and subsequent fiber burning by means of pyrolytic light detection. Hence the laser is automatically stopped before the fiber was over heated and damaged. We therefore decided to use a sterile bare-fiber (0.4 mm core diameter, 12 m length) instead of a diffusing tip. This reduced the risk of bleeding when placing needles in highly vascular lesions. The disadvantage of relatively small affected volumes was compensated for by generating multiple thermal lesions within one CVM. MR imaging before, during, and after ILT was performed on a 0.2 Tesla system (Magnetom OPEN, Siemens, Germany) using a large standard surface coil.

Interstitial Laser Therapy

After MR-guided marking of the skin, the entry site was sterilized and the coil walls were sterilely draped. The titanium alloy needle (diameter 14 Gauge, length 100 mm; Somatex, Germany) was advanced under MR guidance until the tip was positioned as distal as possible from the insertion site. Finally, the laser fiber was introduced and the needle withdrawn. The selection of a distal fiber position in the first place allowed subsequent removal of the laser fiber in small steps. This technique permits coagulation of the whole puncture channel and effectively avoids secondary bleeding. The patients received between 4–19 subsequent laser applications at various positions in order to cover a large volume of the CVM. The primary laser power ranged from 4–6 watts, depending on the preoperative perfusion rate and the intraoperative thermal sensitivity of the tissue. If preoperative CCDS showed no- or low perfusion, initial laser application was started with 4 watts. In CVMs with medium and high perfusion, the selected laser power was 5 and 6 watts, respectively. The laser power was assumed to be adapted after one application, if we saw an increasing reversible thermic effect in the periphery, combined with a small irreversible effect near the fiber tip. When only the irreversible effect occurred, the laser power was reduced in steps of 1 watt before the next application was started in the same CVM. If we saw neither reversible nor irreversible MR changes, the power was too low and was consequently increased by 1 watt. The therapy was stopped at one location if no further signal reduction was observed over a period of 2 minutes or if the laser automatically stopped because of LPS. Thus application time differed from patient to patient and ranged between 2–14 minutes (mean: 6 minutes).

MR-Imaging

Conventional T1-weighted spin echo sequences (TR: 450 ms TE: 5 ms, matrix: 256 × 256, layer: 7–10 mm, 2 signals acquired) and T2-weighted turbo spin echo sequences (TR: 5,000 ms, TE: 117 ms, matrix: 256 × 256, layer: 7–10 mm, 1 signal acquired) were obtained plain in the transverse and sagittal or coronal planes for all patients pre- and postoperatively.

Optimal entry position and angle to the lesion were determined by an external marker and a biplanar short gradient echo sequence adjacent to the axis of the needle (FLASH, TR: 66 ms TE: 9 ms, FA: 80°, matrix: 256 × 256, layer: 10 mm, 1 signal acquired). For the interactive MR-guided puncture a gradient echo sequence with three slices parallel to the needle course was applied (FLASH, TR: 66 ms, TE: 9 ms, FA: 80°, matrix: 256 × 256, layer: 10 mm, measuring time: 10 seconds, 1 signal acquired). Targeting success was confirmed by acquiring an additional plane along the needle orthogonal to the guiding plane.

To monitor ILT, T1-weighted gradient echo (TR: 132 ms, TE: 9 ms, FA: 80°, matrix: 256 × 256, layer: 10 mm, measuring time: 19 seconds, 1 signal acquired) and fast spin echo sequences (TR: 540 ms, TE: 24 ms, echo train: 5, matrix: 256 × 256, layer: 10 mm, measuring time: 18 seconds, 1 signal acquired) were repeatedly acquired during and after laser application. The T1-weighted images were analyzed for regions with signal intensity changes. The maximum area of signal reduction was on-line measured in the central plane using scanner image software.

MR follow-up studies using the above mentioned T1- and T2-weighted sequences were performed immediately ($n = 20$), after 48 hours ($n = 13$), and after 6 weeks ($n = 17$) after ILT. The

TABLE 2. Treatment Summary and Follow-up

Child	T2-Volume of CVM Before ILT	T2-Volume of CVM 6 weeks after ILT	Applications (Number)	Energy[a] (Joule/d = 10–15)	T-1 Volume treated cm^3	T-1 Volume treated Percent	Clinical outcome
1	712	—	6	900	38	5.3	Partial improvement
2	1478	1951	6	1665	118	8.0	No improvement, continued proliferation
3	862	694	16	450	57	6.6	Partial improvement
4	818	—	7	320	92	11.2	Substantial improvement
5	987	872	13	1600	128	12.9	Substantial improvement
6	106	143	7	1800	28	26.9	Partial improvement, continued proliferation
7	201	166	4	1200	28	14.1	Partial improvement
8	670	526	6	1200	86	12.9	Substantial improvement
9	339	121	8	1400	33	9.6	Substantial improvement
10	283	200	4	1000	36	12.7	Partial improvement
11	652	400	11	800	133	20.4	Partial improvement
12	1257	987	19	2715	97	7.7	No improvement
13	1150	1050	12	1000	50	4.3	Partial improvement
14	200	149	11	1344	68	34.1	Substantial improvement
15	210	—	4	1000	35	16.4	Partial improvement
16	143	111	9	991	77	54.3	Partial improvement
17	271	182	6	788	89	32.8	Substantial improvement
18	88	71	6	862	37	42.3	Substantial improvement
19	7019	6850	4	1250	123	1.8	Partial improvement
20	4396	—	11	850	51	1.2	Partial improvement

[a]Mean energy to change T1-weighted MRI by a diameter of 10–15 mm around the fiber tip.

total volumes of the vascular lesions were determined before and 6 weeks after therapy (Table 2). The posttherapeutic images were compared to the on-line images acquired during laser application. No other therapy was performed during the 6 week follow-up.

RESULTS

Passive tip tracking through the titanium alloy provided optimal needle positioning in all applications (Fig.1). Needle repositioning was successfully performed based on the thermal effect recorded by on-line MR-imaging.

Intraprocedural T1-weighted scans revealed signal reduction in 149 of 165 laser applications. The hypo-intense region increased over time with a maximum diameter of 27 mm. This dynamic temperature effect was observed in 119 of 165 cases (Fig. 2). During 42 applications an additional steep signal decrease at the fiber tip was observed which remained stable during laser application and corresponded well with the T1-weighted follow-up examination. Posttherapeutic fiber inspection led to the conclusion that this effect was due to carbonization at the fiber tip. In 30 procedures a strong irreversible signal loss at the fiber tip was observed without any peripheral reaction. This was assumed to indicate vaporization. A laser application was stopped if variations in signal intensity were found beneath the carotid artery (n = 3), aorta (n = 1), caval vein (n = 2), ureter (n = 1), or sciatic and fibularis nerve (n = 3). All hypointense regions showed a size reduction after switching off the laser, being 32% to 76% in the T1-weighted 3 minute follow-up images as compared to the maximum diameter measured directly at the end of the procedure. Also, the acquired T2-weighted sequences immediately after therapy revealed alterations, showing good correlation with the intraprocedural T1-weighted images. The preoperative CVM volume ranged from 88 to 7,019 cm^3 (Table 2). The 6 week follow-up revealed a reduction in tumor size in 14 of 16 patients (mean 76.1%). In four of these patients the symptoms were completely resolved after therapy (patients 8, 9, 17, and 18). In 2 of 16 patients, the 6 week follow-up revealed an increase in tumor size despite ILT (mean 134%).

Complications occurred in three patients. Two suffered from a small superficial area of skin slough which healed with conservative treatment. One fiber was broken during a treatment because the light guide protection system was not avail-

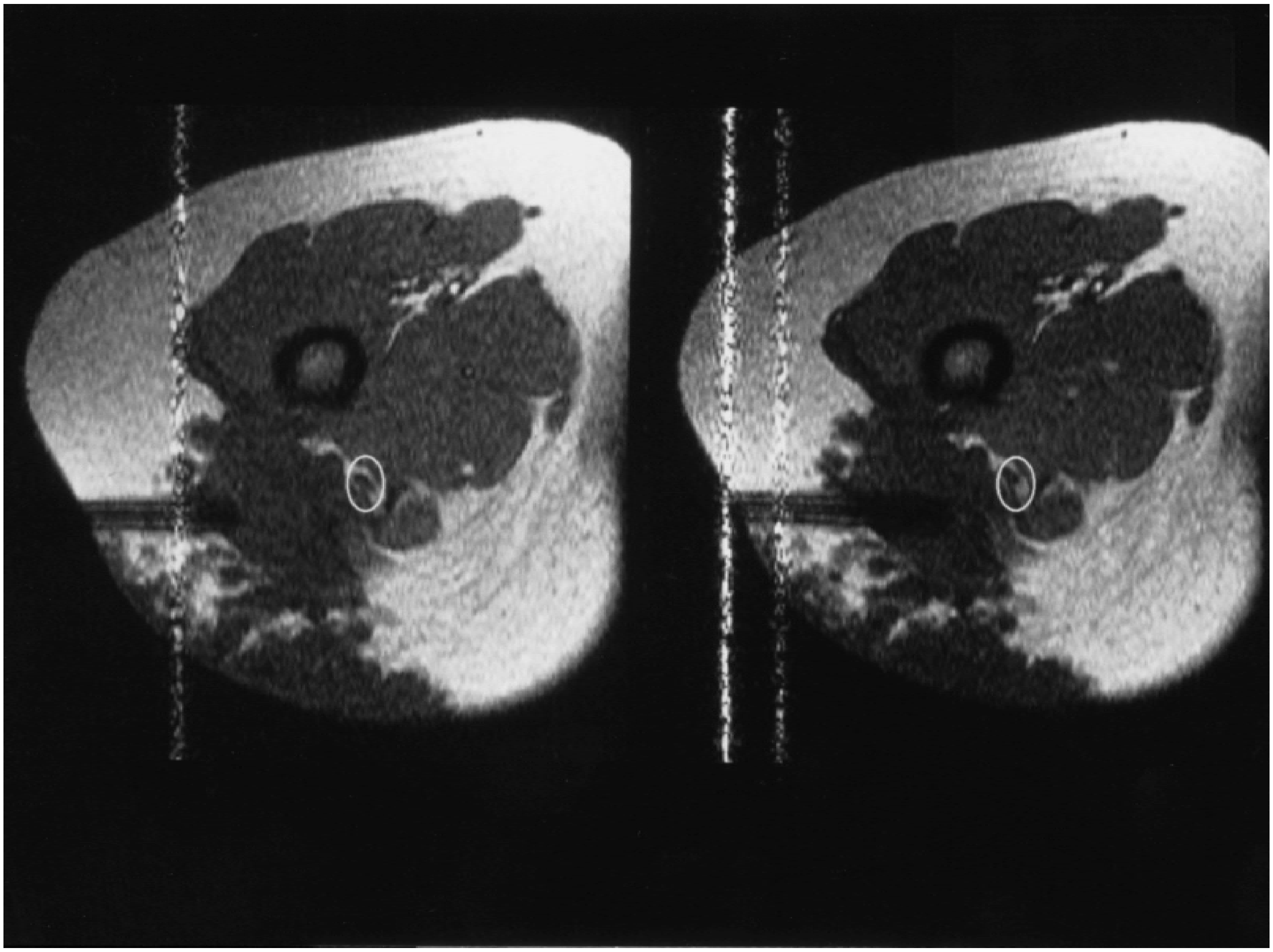

Fig. 1. Puncture. The vascular malformation penetrates the dorsal thigh muscle. The puncture needle is positioned by passive tip tracking at a precise distance to the endangered sciatic nerve (White Oval).

able this day. We did not observe intraoperative or secondary bleeding complications. The period of anesthesia ranged from 100 to 360 minutes (mean: 200 minutes), the treatment period ranged from 60 to 280 minutes (mean: 150 minutes). The total laser application time varied between 12 and 93 minutes (mean: 45 minutes). On average, first MR-signal alterations were found after 120 seconds. The maximum volume of a single laser lesion was 6 cm^3, measured immediately after the treatment. To find an MR-signal alteration with a diameter of 10–15 mm, an energy of 966 Joule was required if no preoperative blood flow was found, 1,063 Joules were applied at low perfusion, 1,145 Joules at medium flow and 1,360 Joules at high perfusion. Hence there is a significant correlation between required energy to reach a certain thermal reaction and tumor blood perfusion.

DISCUSSION

All laser interventions revealed temperature related variations in the MR-signal intensity. The amount of energy required to effect a certain diameter in signal loss was not precisely predictable, but was comparable to that found in vivo in highly vascularized tissues [26]. The sensitivity to the laser energy depended on structure, cell type, color, lacunarization, and perfusion of the CVM. As a result the dynamic temperature behavior of most tissue parameters required a modification of the laser power during the course of therapy. The laser power was set correctly if the region of signal loss increased continuously around the fiber tip. A small blood flow in the CVM led to a more sensitive reaction to the laser radiation which also varied from position to position in mixed haemolymphatic forms. A degenerative adiposis

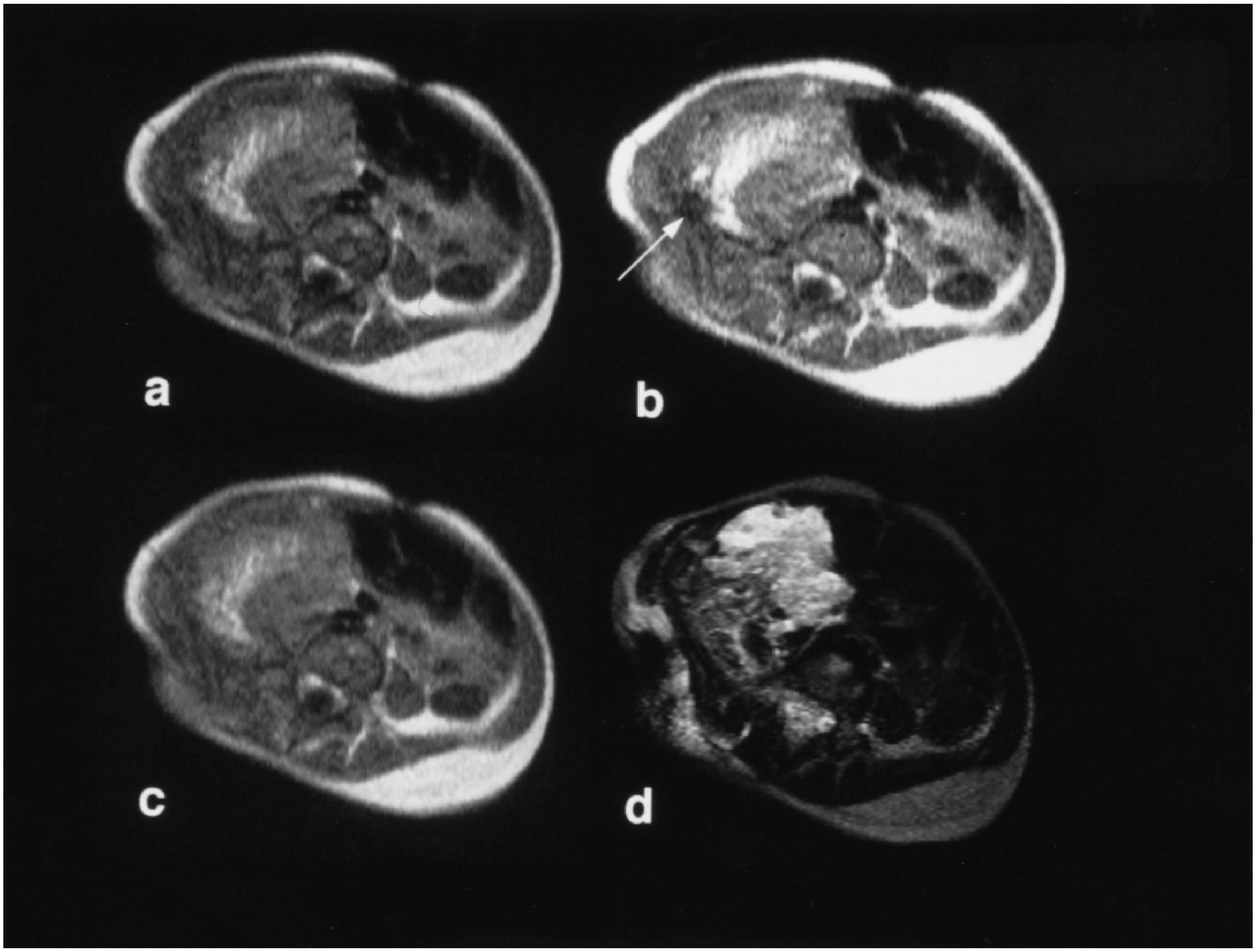

Fig. 2. Reversible MR-signal loss in a CVM of the right retroperitoneum **a:** T1: puncture above the pelvis and introduction of the bare fiber. **b:** T1: 80 seconds ILT at 5 watts. The arrow indicates the hypo-intense region. **c:** T1: 180 seconds after ILT. The hypo-intense region totally disappeared. **d:** T2: The 6 week follow-up shows a reduced signal intensity in the treated dorsal region of the CVM.

within the CVM reduced its reaction to ILT. Even lymphatic CVMs with a small hemoglobin content can be treated by ILT, as they exhibit significant thermal MR-signal changes. The treated volume can be enlarged by slowly withdrawing the fiber during laser application under open MR-control [27].

A high intensity loss at the fiber tip indicated charring, leading to a high absorption of the carbonized tissue. If this occurred, the therapy was manually stopped or was automatically interrupted by the light guide protection system. Then the fiber was evaluated, repositioned, and the laser power was adapted. Frequent fiber repositioning revealed the disadvantage of the bare fiber technique. Nevertheless, for the first 20 patients the use of the bare fiber was indicated because the interstitial technique had to be optimized with a minimal risk of bleeding. But the maximum volume of a vascular malformation treated with the bare fiber is limited for practical reasons. Therefore the use of other application systems seems to be indicated for voluminous and highly perfused CVMs. Vogl et al. used a diffusing applicator with a length of 20 mm in combination with a temperature stable protecting catheter in order to treat large tumors in the liver [5]. They were able to control tumors of up to 2 cm in diameter with a single laser application. Comparable lesion sizes were reported by Muschter et al. for the laser treatment of the prostate, using a circumferentially radiating applicator [8]. The interstitial technique could potentially be improved by applying the simultaneous application of multiple fi-

bers. This technique provides lesion volumes between 3.7 and 12.6 cm^3 with four fibers but requires a high number of interventions [28]. By now, the largest volumes of coagulation have been achieved with diffusing applicators introduced into a cooled catheter system. In vitro experiments showed coagulation volumes of up to 30 cm^3 in porcine liver [29–32]. The application of the cooled diffusing tip for the MR-controlled treatment of liver tumors revealed a significant increase in lesion volume in comparison to the noncooled laser applicators [32]. Consequently further investigations of ILT for CVM will focus on the application of cooled laser applicators in order to reduce the treatment time and improve the patient outcome.

Disadvantages of the open MR-guided laser procedure are an increased infection risk, expensive equipment, and extended anesthesia periods. Consequently, the MR-guided ILT for CVM should be restricted to selected regions. Although we have no histological proof of the correlation between MR-signal changes and irreversible damage of the malformations, ILT controlled in an open 0.2 Tesla MR-unit is a promising alternative treatment modality for CVMs, coming closer to the "crux therapeuticum" of deep vascular malformations.

ILT might supplement other procedures such as embolization or surgical resection by offering a further method for the treatment of recurrences or remaining tumor tissue. It is expected that ILT could also be applied as a standalone procedure for some forms of CVM, particularly extratruncular malformations with infiltrating growth.

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